Remarks

A. Claims in the Case

Claims 50, 76, and 98-118 are pending in the case. Claims 50, 76, and 98-118 have been rejected. Claims 50 and 76 have been amended.

B. The Claims Are Not Obvious Over Walt in view of Felder Pursuant To 35 U.S.C. § 103(a)

Claims 50, 76, and 98-118 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,327,410 to Walt et al. (hereinafter "Walt") in view of U.S. Patent No. 6,232,066 to Felder et al. (hereinafter "Felder"). Applicant respectfully disagrees with these rejections.

In order to reject a claim as obvious, the Examiner has the burden of establishing a *prima facie* case of obviousness. *In re Warner et al.*, 379 F.2d 1011, 154 USPQ 173, 177-178 (C.C.P.A. 1967). To establish a *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974), MPEP § 2143.03.

Amended claim 50 states:

> a plurality of sensing elements having a predetermined shape, wherein a first portion of the sensing elements are configured to produce a signal in the presence of a first analyte and wherein a second portion of the sensing elements are configured to produce a signal in the presence of the second analyte, and wherein the first and second portions of the sensing elements have predetermined shapes, and wherein the shape of the first portion of the sensing elements is different from the shape of the second portion of the sensing elements;
>
> placing the sensing elements in a liquid composition; and

curing the liquid composition to form a supporting member, wherein the sensing elements are at least partially embedded within the cured liquid composition.

Walt alone or in combination with Felder does not appear to teach or suggest the combination of features of the claims, including, but not limited to, the feature of; "curing the liquid composition to form a supporting member, wherein the sensing elements are at least partially embedded within the cured liquid composition."

Walt appears to teach modifying a substrate, the substrate having sites appropriate for attachment of discrete particles to a surface of the substrate such that the particles do not move during the course of the assay. The surface of the discrete particles may be modified. The particles may be attached to the surface of the substrate by forming a film over the particles, which holds the particles in place. Walt states:

> The compositions comprise a substrate. By "substrate" or "solid support" or other grammatical equivalents herein is meant any material that can be modified to contain discrete individual sites appropriate for the attachment or association of beads and is amenable to at least one detection method. As will be appreciated by those in the art, the number of possible substrates are very large, and include, but are not limited to, glass and modified or functionalized glass, plastics (including acrylics, polystyrene and copolymers of styrene and other materials, polypropylene, polyethylene, polybutylene, polyurethanes, Teflon.TM., etc.), polysaccharides, nylon or nitrocellulose, resins, silica or silica-based materials including silicon and modified silicon, carbon, metals, inorganic glasses, plastics, optical fiber bundles, and a variety of other polymers. In general, the substrates allow optical detection and do not appreciably fluoresce.
> (Walt, column 5, lines 32-47)

> In a preferred embodiment, the surface of the substrate is modified to contain chemically modified sites, that can be used to attach, either covalently or non-covalently, the microspheres of the invention to the discrete sites or locations on the substrate. "Chemically modified sites" in this context includes, but is not limited to, the addition of a pattern of chemical functional groups including amino groups, carboxy groups, oxo groups and thiol groups, that can be used to covalently attach microspheres, which generally also contain corresponding reactive functional groups; the addition of a pattern of adhesive that can be used to

bind the microspheres (either by prior chemical functionalization for the addition of the adhesive or direct addition of the adhesive); the addition of a pattern of charged groups (similar to the chemical functionalities) for the electrostatic attachment of the microspheres, i.e. when the microspheres comprise charged groups opposite to the sites; the addition of a pattern of chemical functional groups that renders the sites differentially hydrophobic or hydrophilic, such that the addition of similarly hydrophobic or hydrophilic microspheres under suitable experimental conditions will result in association of the microspheres to the sites on the basis of hydroaffinity. For example, the use of hydrophobic sites with hydrophobic beads, in an aqueous system, drives the association of the beads preferentially onto the sites. As outlined above, "pattern" in this sense includes the use of a uniform treatment of the surface to allow attachment of the beads at discrete sites, as well as treatment of the surface resulting in discrete sites. As will be appreciated by those in the art, this may be accomplished in a variety of ways. (Walt, column 6, line 48 through colum 7, line 10).

FIG. 1 illustrates the construction of a bead or microsphere 10 according to the principles of the present invention. In common with the prior art, the microsphere 10 is given a bioactive agent 12, which is typically applied to the microsphere's surface. The bioactive agent is designed so that in the presence of the analyte(s) to which it is targeted, an optical signature of the microsphere, possibly including region surrounding it, is changed.

It should be noted that a key component of the invention is the use of a substrate/bead pairing that allows the association or attachment of the beads at discrete sites on the surface of the substrate, such that the beads do not move during the course of the assay.
(Walt, column 7 lines 20-54)

Microspheres 10 may then be fixed into the wells 250 by using a dilute solution of sulfonated Nafion that is dripped over the end. Upon solvent evaporation, a thin film of Nafion was formed over the Microspheres which holds them in place.....A smilar approach can be employed with different polymers. (Walt, column 18, lines 55-66).

Walt appears to teach the formation of cavities that are used to hold particles. The cavities are formed within a supporting material. Walt further appears to teach that the particles may be coupled to the supporting material using a polymer. Applicant submits, the features of the claims including, but not limited to, the features of, "curing the liquid composition to form a supporting member, wherein the sensing elements are at least

partially embedded within the cured liquid composition" are not taught or suggested by Walt.

Felder appears to teach modifying a surface and attaching anchors and/or linkers to the surface. Felder appears to teach that the shape of the surface is not critical. Felder states:

> Any compatible surface can be used in conjunction with this invention. The surface (usually a solid) can be any of a variety of organic or inorganic materials or combinations thereof, including, merely by way of example, plastics such as polypropylene or polystyrene; ceramic; silicon; (fused) silica, quartz or glass, which can have the thickness of, for example, a glass microscope slide or a glass cover slip; paper, such as filter paper; diazotized cellulose; nitrocellulose filters; nylon membrane; or polyacrylamide gel pad. Substrates that are transparent to light are useful when the method of performing an assay involves optical detection. In a preferred embodiment, the surface is the plastic surface of a multiwell e.g. tissue culture dish, for example a 24-, 96-, 256-, 384, 864- or 1536-well plate (e.g. a modified plate such as a Corning Costar DNA Bind plate). Anchors can be associated, e.g. bound, directly with a surface, or can be associated with one type of surface, e.g glass, which in turn is placed in contact with a second surface, e.g. within a plastic "well" in a microfiter dish. The shape of the surface is not critical. It can, for example, be a flat surface such as a square, rectangle, or circle; a curved surface; or a three dimensional surface such as a bead, particle, strand, precipitate, tube, sphere; etc.
> (Felder, column 4, line 63 through column 5 line 14).

Applicant's specification states,

> The sensing elements may be formed using a variety of techniques. Generally, the sensing elements are formed from a composition which is subsequently cured. The curing may be conducted to impart a predefined shape to the sensing element. This shape may be used to identify the specific sensing element. Techniques that may be used to fabricate sensing elements include, but are not limited to, contact lithography, projection lithography, imprint lithography or micromolding based on surface wetting.
>
> Contact lithography uses photomask templates to cross link liquid monomer materials into sensing elements on an inert substrate (e.g., a glass microscope slide). Referring to FIGS. 2 and 3, mask 210 that includes one or more openings 215 having a predetermined shape is placed on inert substrate 220. Mask 210 may include, but is not limited to, transparencies (such as those used in

> a laser printer), 35mm slide film, or patterned chrome on a quartz plate. A secondary mask (not shown) may be placed between mask 210 and composition 230 to protect mask 210. Inert substrate 220 may be, for example, a white Teflon dish. Inert substrate 220 may include cavity 225. Cavity 225 may range from about 0.25-1.0 mm deep. The depth of cavity 225 may control the thickness of the sensing elements. It may be advantageous to use a non-reflective pan instead of a white Teflon dish. The non-reflective pan may reduce UV scattering allowing smaller, higher resolved sensing elements to be formed. Composition 230 used to form the sensing elements may be disposed in cavity 225. Activating light may be applied to the composition disposed within cavity 225 to cure the composition. As used herein "activating light" means light that may affect a chemical change. Activating light may include ultraviolet light (e.g., light having a wavelength between about 300 nm to about 400 nm), actinic light, visible light or infrared light. Generally, any wavelength of light capable of affecting a chemical change may be classified as activating. Chemical changes may be manifested in a number of forms. A chemical change may include, but is not limited to, any chemical reaction that causes a polymerization or a cross-linking reaction to take place. The activating light may be passed through the mask prior to reaching the composition. In this manner the composition may be cured to form the sensing elements. The portions of the composition that are exposed to the activating light may be cured while the unexposed portions of the composition may be substantially uncured. In this manner sensing elements having a shape defined by the openings in mask 210 may be produced.
> (Specification, page 12, line 13 through page 13, line 17).

Applicant submits, the features of the claims including, but not limited to, the features of, "curing the liquid composition to form a supporting member, wherein the sensing elements are at least partially embedded within the cured liquid composition" are not taught or suggested by Walt alone or in combination with Felder. As such, Applicant submits claim 50 and the claims dependent thereon (claims 98-108) are patentable over Walt in view of Felder.

Claim 76 includes a combination of features that relate to a method of sensing multiple analytes in a fluid including, but not limited to, the feature of, "determining the shape of the sensing elements that undergo a spectroscopic change."

The Office Action states, "claim 76 differs by reciting that the method employs sensing elements (beads) of different shapes wherein the sensing element undergoing a spectroscopic

change is identified by its shape. The reference of Felder et al. discloses that it is known in the art to provide analyte detections beads with unique optical signatures or tags wherein the beads can be of different size or shape." Applicant respectfully disagrees.

Applicant submits that Felder teaches away from determining the shape of the sensing element. Felder appears to teach that the shape of the surface that the anchors are associated with is not critical. Felder states, "The shape of the surface is not critical. It can, for example, be a flat surface such as a square, rectangle, or circle; a curved surface; or a three dimensional surface such as a bead, particle, strand, precipitate, tube, sphere; etc" (Felder, column 5, lines 14-15).

Teaching away from art is a *per se* demonstration of lack of obviousness. *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988); *In re Fine*, 837, F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

As such, Applicant submits that there is no motivation in Walt alone or in combination with Felder to teach or such the combination of features of the claims including, but not limited to, the feature of, "determining the shape of the sensing elements that undergo a spectroscopic change."

Obviousness can only be established by "showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teaching of the references." *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).

Applicant submits claim 76 and the claims dependent thereon (claims 109-118) are patentable over Walt in view of Felder.

C. <u>The Claims Are Not Obvious Over Walt in View of Chang et al. Pursuant To 35 U.S.C. § 103(b)</u>

Claims 50, 76, and 98-118 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Walt in view of U.S. Patent No. 6,350,620 to Chang et al. (hereinafter "Chang"). Applicant respectfully disagrees with these rejections.

Claim 50 states in part, "curing the liquid composition to form a supporting member, wherein the sensing elements are at least partially embedded within the cured liquid composition."

For at least the reasons stated above, Applicant submits claim 50 is patentable over Walt. Applicant submits that Chang does not appear to teach or suggest the combination of the features of the claim. Chang appears to teach hot compressing a bar code on a bead and then attaching genes or proteins to the beads. Chang states, "the term 'micro-carrier' used herein refers to a bead marked with a specific bar code, then coated with a layer of bio-molecule binding material" (Change, column 2, lines 56-58).

As such, Applicant submits that the combination of the features of the claim 50 and the claims dependent thereon are not taught by Walt alone or in combination with Chang. Applicant submits that claim 50 and the claims dependent thereon are patentable over Walt in view of Chang.

Claim 76 includes a combination of features that relate to a method of sensing multiple analytes in a fluid including, but not limited to, the feature of, "determining the shape of the sensing elements that undergo a spectroscopic change."

For at least the reasons stated above, Applicant submits claim 76 is patentable over Walt.

The Office Action states, "Chang et al. discloses that it is known in the art to provide analyte detection beads with unique optical signatures or tags wherein the beads can be of different size or shape." Applicant respectfully disagrees.

Chang does not appear to teach or suggest the sensing element undergoing a spectroscopic change. Chang appears to teach labeling an unknown bio-molecule with a fluorescent compound, mixing the labeled bio-molecule with the carrier, and then detecting the fluorescent signal produced by the labeled bio-molecule when the labeled bio-molecule is complementary to or recognizes the micro-carrier. The micro-carrier may be different shapes and sizes. Chang states:

> The method is comprised of the following steps: providing a vial containing numerous micro-carriers with bar code; adding a labeled (for example, fluorescence-labeled) unknown bio-molecule to said vial and mixing (i.e. hybridizing), wherein a signal, such a fluorescence, is obtained when the micro-carrier is complementary with or recognized by the unknown bio-molecule.....identifying said bar code of the signaling micro-carrier by an image recognition system...
> (Chang, column 3 lines 10-21)

Applicant submits that there is no motivation in Walt alone or in combination with Chang to determine the shape of the sensing element that undergoes a spectroscopic change.

Whether or not "a particular combination might be 'obvious to try' is not a legitimate test of patentability." *Id.* at 1599, citing *In re Geiqer*, 815 F.2d 868, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987) and *In re Goodwin*, 576 F.2d 375, 377, 198 USPQ 871, 881 (CCPA 1981). Consequently, it is not permissible for the Examiner to "use hindsight reconstruction to pick and chose among isolated disclosures in the prior art to deprecate the claimed invention." Id. at 1600.

For at least the reasons stated above, Applicant submits that claim 76 and the claims dependent thereon (claims 98-118) are patentable over Walt in view of Chang.

D. The Claims Are Not Obvious Over Walt in View of Ravkin Pursuant To 35 U.S.C. § 103(b)

Claims 50, 76, and 98-118 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Walt in view of U.S. Published Application No. 2003/0008323 to Ravkin et al. (hereinafter "Ravkin"). Applicant respectfully disagrees with these rejections.

Claim 50 states in part, "curing the liquid composition to form a supporting member, wherein the sensing elements are at least partially embedded within the cured liquid composition."

For at least the reasons stated above, Applicant submits claim 50 are patentable over Walt. Applicant submits that Ravkin does not appear to teach or suggest the combination of the features of the claim. Ravkin appears to teach attaching probe molecules to specific and identifiable carriers. Ravkin states, "In use, a composition containing up M^N coded carriers, each formed with a different surface attached compound" (Ravkin, page 9, paragraph 118).

Applicant submits that the combination of the features of claim 50 and the claims dependent thereon are not taught by Walt alone or in combination with Ravkin. As such, Applicant submits claim 50 and the claims dependent thereon are patentable over Walt in view of Ravkin.

Claim 76 includes a combination of features that relate to a method of sensing multiple analytes in a fluid including, but not limited to, the features of, "wherein the sensing elements are at least partially embedded within the supporting member."

For at least the reasons stated above, Applicant submits claim 76 is patentable over Walt.

Ravkin does not appear to teach or suggest the features of the claim including, but not limited to the feature of "determining the shape of the sensing elements that undergo a spectroscopic change." Ravkin appears to teach carriers that have coded indicia and coded positions that are attached to the carriers. The indicia may be used to determine the shape of the carrier. Ravkin states, "the geometry of the carrier may serve as coding indicia" (Ravkin, page 11, paragraph 137) and "a plurality of coded carriers, each having N>1 specified code positions and one of M>1 detectable indicia at each code positions such that each carrier can be identified by one of up to M^N different code combinations" (Ravkin, page 12, paragraph 146).

Applicant submits that there is no motivation or teaching in Walt or Ravkin to combine sensing elements having a first portion is different from the shape of the second portion of the sensing elements with indicia.

Whether or not "a particular combination might be 'obvious to try' is not a legitimate test of patentability." *Id.* at 1599, citing *In re Geiqer*, 815 F.2d 868, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987) and *In re Goodwin*, 576 F.2d 375, 377, 198 USPQ 871, 881 (CCPA 1981).

Applicant submits that the features of the claim including, but not limited to, the features of, "determining the shape of the sensing elements that undergo a spectroscopic change." are not taught or suggested by Walt alone or in combination with Ravkin. As such, Applicant submits claim 76 and the claims dependent thereon are patentable over Walt in view of Ravkin.

E. <u>The Claims Are Not Obvious Over Schmid et al.</u>

Claim 76 and 109-118 have been provisionally rejected under the judicially created doctrine of double patenting over claims 117-143 of co-pending U.S. Patent Application No. 10/832,469 to Schmid et al. in view of Walt. Applicant respectfully disagrees with this rejection.

If, however, the claims are allowed, Applicant will consider filing a terminal disclaimer disclaiming the terminal part of the statutory term of any patent granted on the instant application

which would extend beyond the expiration date of the full statutory term of co-pending U.S. Patent Application 10/832,469.

F. Many Of The Claims Are Separately Patentable

The Examiner is also respectfully requested to separately consider each of the dependent claims for patentability. Many of the dependent claims in addition to those mentioned above are independently patentable.

For instance, claim 98 states in part "wherein forming a sensing element comprises polymerizing a monomer composition." Applicant submits that this feature, in combination with the features of the independent claim 50 does not appear to be taught or suggested by the cited art.

Claim 99 states in part, "wherein placing the sensing element in a liquid composition comprises placing the sensing elements at the surface of the liquid composition." Applicant submits that this feature, in combination with the features of the independent claim 50 does not appear to be taught or suggested by the cited art.

Claim 100 states in part, "wherein the sensing element comprises a polymer." Applicant submits that this feature, in combination with the features of the independent claim 50 does not appear to be taught or suggested by the cited art.

Claim 101 states in part, "wherein the sensing element comprises a polyethylene glycol hydrogel." Applicant submits that this feature, in combination with the features of the independent claim 50 does not appear to be taught or suggested by the cited art.

Claim 102 states in part, "wherein forming the sensing element comprises coupling a receptor to a polymeric body, and wherein the receptor is configured to produce a signal when

the sensing element interacts with the analyte during use." Applicant submits that this feature, in combination with the features of the independent claim 50 does not appear to be taught or suggested by the cited art.

Claim 103 states in part, "wherein forming the sensing element comprises coupling a receptor to a polymeric body, and wherein the polymeric body comprises a non-spherical shape." Applicant submits that this feature, in combination with the features of the independent claim 50 does not appear to be taught or suggested by the cited art.

Claim 104 states in part, "wherein forming the sensing element comprises coupling a receptor to a polymeric body, and wherein the polymeric body comprises a polyethylene glycol polymer." Applicant submits that this feature, in combination with the features of the independent claim 50 does not appear to be taught or suggested by the cited art.

Claim 105 states in part, "wherein forming the sensing element comprises coupling a receptor to a polymeric body, and wherein the polymeric body comprises a polyethylene glycol diacrylate." Applicant submits that this feature, in combination with the features of the independent claim 50 does not appear to be taught or suggested by the cited art.

Claim 106 states in part, "wherein forming the sensing element comprises coupling a receptor to a polymeric body, and wherein the receptor is coupled to an outer surface of the polymeric body." Applicant submits that this feature, in combination with the features of the independent claim 50 does not appear to be taught or suggested by the cited art.

Claim 107 states in part, "wherein forming the sensing element comprises coupling a receptor to a polymeric body, and wherein the receptor is at least partially encapsulated within the polymeric body." Applicant submits that this feature, in combination with the features of the independent claim 50 does not appear to be taught or suggested by the cited art.

Claim 108 states in part, "wherein forming the sensing element comprises coupling a receptor to a polymeric body, and wherein the receptor comprises a nucleic acid." Applicant submits that this feature, in combination with the features of the independent claim 50 does not appear to be taught or suggested by the cited art.

Claim 109 states in part, "wherein the sensing element comprises a polymer." Applicant submits that this feature, in combination with the features of the independent claim 76 does not appear to be taught or suggested by the cited art.

Claim 110 states in part, "wherein the sensing element comprises a polyethylene glycol hydrogel." Applicant submits that this feature, in combination with the features of the independent claim 76 does not appear to be taught or suggested by the cited art.

Claim 111 states in part, "wherein the sensing element comprises a receptor, and wherein the receptor is configured to produce a signal when the sensing element interacts with the analyte during use." Applicant submits that this feature, in combination with the features of the independent claim 76 does not appear to be taught or suggested by the cited art.

Claim 112 states in part, "wherein the sensing element comprises a receptor coupled to a polymeric body." Applicant submits that this feature, in combination with the features of the independent claim 76 does not appear to be taught or suggested by the cited art.

Claim 113 states in part, "wherein the sensing element comprises a receptor coupled to a polymeric body, and wherein the polymeric body comprises a non-spherical shape." Applicant submits that this feature, in combination with the features of the independent claim 76 does not appear to be taught or suggested by the cited art.

Claim 114 states in part, "wherein the sensing element comprises a receptor coupled to a polymeric body, and wherein the polymeric body comprises a polyethylene glycol polymer."

Applicant submits that this feature, in combination with the features of the independent claim 76 does not appear to be taught or suggested by the cited art.

Claim 115 states in part, "wherein the sensing element comprises a receptor coupled to a polymeric body, and wherein the polymeric body comprises a polyethylene glycol diacrylate." Applicant submits that this feature, in combination with the features of the independent claim 76 does not appear to be taught or suggested by the cited art.

Claim 116 states in part, "wherein the sensing element comprises a receptor coupled to a polymeric body, and wherein the receptor is coupled to an outer surface of the polymeric body." Applicant submits that this feature, in combination with the features of the independent claim 76 does not appear to be taught or suggested by the cited art.

Claim 117 states in part, "wherein the sensing element comprises a receptor coupled to a polymeric body, and wherein the receptor is at least partially encapsulated within the polymeric body." Applicant submits that this feature, in combination with the features of the independent claim 76 does not appear to be taught or suggested by the cited art.

Claim 118 states in part, "wherein the sensing element comprises a receptor coupled to a polymeric body, and wherein the receptor comprises a nucleic acid."

G. Additional Remarks

Based on the above, favorable consideration is respectfully requested.

If an extension of time is required, Applicant hereby requests the appropriate extension of time. Should any fees be required, or if any fees have been overpaid, the Commissioner is authorized to appropriately charge or credit those fees to Meyertons, Hood, Kivlin, Kowert & Goetzel, P.C. Deposit Account No. 50-1505/5119-07301/EBM.

Respectfully submitted,

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